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Case Report

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A Case Report and Literature Analysis of Dorsal Hand-Foot Syndrome Induced with Albumin-Bound Paclitaxel

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Abstract

Dorsal hand-foot syndrome (dorsal HFS), also known as an atypical presentation of hand-foot syndrome (HFS) on the dorsum of hands and feet. Only taxanes have been reported to develop dorsal HFS according to the current literature reviews. Nanoparticle albumin-bound paclitaxel (nabpaclitaxel) as a new type of taxanes, however, there are no covers about this dermatologic toxicity syndrome. This article will expound a rare dermatology adverse reaction induced by nab-paclitaxel and review dorsal hand-foot syndrome from clinical manifestations, differential diagnosis, possible pathogenesis and potential therapies. For clinicians, it is crucial to quickly, accurately identify the dorsal HFS and clarify its mechanism for preventing the dorsal hand foot syndrome, selecting a reasonable treatment scheme for patients and improving the quality of life of patients.

Keywords: Dorsal hand-foot syndrome; Nanoparticle albumin-bound paclitaxel; Antidiastole; Management.

Introduction

Dorsal hand-foot syndrome (dorsal HFS) is an adverse reaction induced with taxanes, mainly characterizes as symmetrical, pleomorphic purplish red plaques, pigmentation, desquamation, pain, itching and swelling in the skin of the back of the hand and foot, which can occasionally involve the palmoplantar part [1-4]. In reviewing the literatures of chemotherapy related dermal toxicity, dorsal HFS is generally caused by paclitaxel and docetaxel [1,2,5, 6]. And the incidence of docetaxel-induced HFS is approximately 10%, more common than paclitaxel [7]. However, there are no covers about nab-paclitaxel induced with dorsal HFS. Furthermore, this untoward dermal toxicity on the dorsal skin of hands and feet may be classified as HFS in some case reports. At present, there is no systematic descriptions of the pathogenesis, diagnosis and treatment of dorsal HFS. In this review, we will present a case of dorsal hand-foot syndrome that induced by nanoparticle albumin-bound paclitaxel, and will discuss from the aspects of differential diagnosis, possible pathogenesis and managements.

Case presentation

A 75-year-old female with advanced gastric cancer and peritoneal metastasis was admitted to our hospital. In terms of treatment scheme selection, according to multi-disciplinary team's advice, she was recommended to use chemotherapeutic drugs to treat illness. And since July 14,2020, this patient has been treated with nab-paclitaxel combined tegafur (Table 1). And prior to each period, she was premedicated with 5 mg dexamethasone, 5 mg tropisetron, 50 mg diphenhydramine, and 150 mg fosapitan.

On cycle 6 day 14, the patient complained of pain with erythema or violaceous papules, pruritus, swelling and paresthesia on her

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dorsum of feet, that prevented her from pursuing activities of daily life (Figure 2A). To alleviate these unwell symptoms, she received palliative therapies in another hospital and subsequently returned to our hospital one month later than originally scheduled. After admission, she underwent physical examination and results revealed tender erythema, purplish red papules and plaques, mildly desquamation and edema on her dorsal feet skin (Figure 2B). She denied the history of taking other drugs and contacting allergens during chemotherapy. Combined with the patient's clinical symptoms and treatment process, in order to determine whether this series of symptoms of the patient are adverse reactions of chemotherapy drugs or diseases of blood system, the patient was further tested by routine blood test, liver function test and coagulation test, and no abnormality was found in the test results (Table 2). Therefore, subcutaneous hemorrhage caused by diseases of blood system was excluded, and skin toxicity caused by chemotherapy drugs was considered. And her symptoms were more likely to be considered as dorsal hand-foot syndrome, which caused by nab-paclitaxel.

According to the grade of toxic and side effects of chemotherapeutic drugs, her symptoms were considered as grade 3 or 4 (Table 3) Adverse Event (AE) [8]. Due to the efficacy of the current chemotherapy regimen was evaluated as stable disease (shrinkage), so according to AE treatment strategies (Figure 2), we withdrew albumin-paclitaxel and selected tegafur as her maintenance treatment [7,9]. She was also advised to undergo palliative measures by taking low dose corticosteroids, using hirudoid cream, wearing soft clothes, and reducing skin friction on feet. We also followed up with this patient. During the follow-up period, these uncomfortable reactions on the patient's dorsum of feet gradually improved, and after the sixth courses of teggio maintenance treatment, her feet skin returned to be normal (Figure 2C). The patient's follow-up results further confirmed that albumin-paclitaxel was the offending agent.

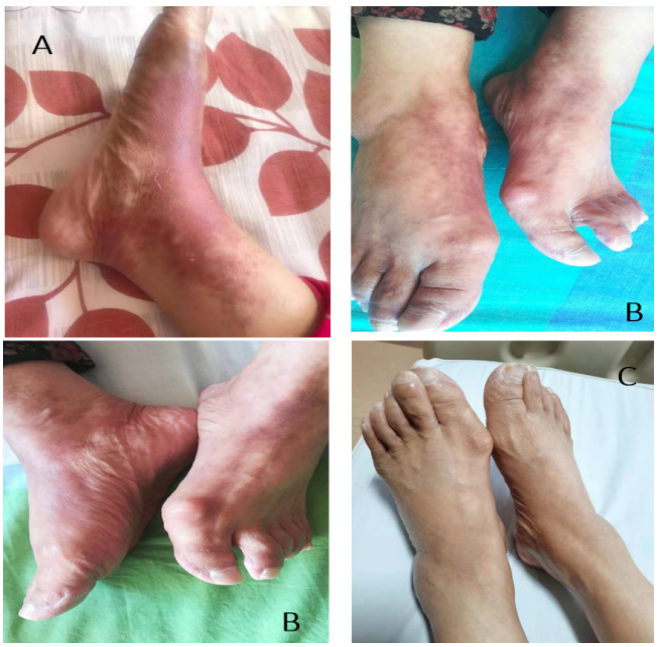

Figure 1: Appearance of skin lesions on the dorsum of feet.

Table 1: The patient's treatment strategy and treatment course.

Cycle	Day	Treatment
	D1	albumin-bound paclitaxel 260 mg/m² peritoneal perfusion
	D8	albumin-bound paclitaxel 260 mg/m² intravenous
Cycle 1-2	D1-D14	Tegafur 80mg/m² oral
	D1	albumin-bound paclitaxel 260 mg/m² intravenous
	D8	albumin-bound paclitaxel 260 mg/m² intravenous
Cycle 3-6	D1-14	Tegafur 80 mg/m² oral

Table 2: The patient's laboratory test results.

December 12,2020						
Blood routine	RBC: 3.78 x 10^{12}/L	HGB: 114 g/L	PLT: 192 x 10^{9}/L	WBC: 3.96 x 10^{9}/L		
Coagulation routine	TT: 17.0s	APTT: 26.4s	PT: 10.4s	INR: 0.88	PT	FB
					A: 130%	G: 4.17 g/L
Liver function	TBIL: 9.1 umol/L	DBIL: 1.7 umol/L	IBIL: 7.4 umol/L	Globulin: 24.7 g/L		

Table 3: Classification criteria of HFS according to NCI and WHO.

Grade	NCI	WHO
1	Minimal skin changes or dermatitis (rash, edema, hyperkeratosis) without pain	Dysesthesia/paresthesia, tingling in hands and feet
2	Skin changes (peeling, blisters, bleeding, cracks, edema, hyperkeratosis) with pain, limiting instrumental ADL	Discomfort in holding objects or in walking, edema or/and erythema without pain
3	Severe skin changes (peeling, blisters, bleeding, cracks, edema, hyperkeratosis) with pain; limiting self-care ADL	Painful erythema and edema in palms and soles, and around fingernails and toenails
4		Desquamation, ulceration, blistering, severe pain

NCI: the American National Cancer Institute; WHO: the World Health Organization; ADL: activities of daily life.

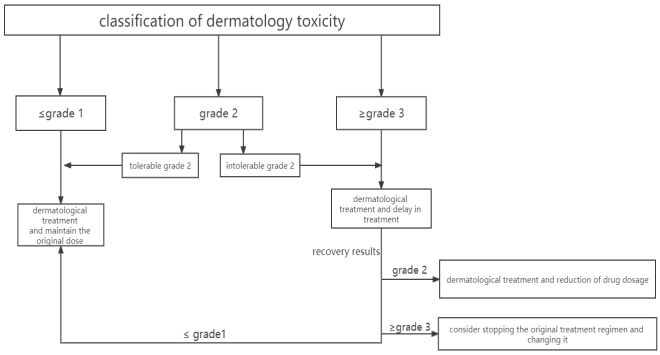

Figure 2: The managements of cutaneous adverse reactions.

Discussion

Among the side effects related to chemotherapeutic drugs, dermatological toxicity is the most common adverse reaction. Common cutaneous adverse reactions include eruption, Hand-Foot Syndrome (HFS), dorsal hand-foot syndrome, Periarticular Thenar Erythema With Onycholysis (PATEO), and Hand Foot Syndrome Reaction (HFSR). Hand-Foot Syndrome (HFS), one of the most universal adverse effects commonly characters as palmoplantar numbness, tingling, burning pain, erythema, pigmentation, with or without edema on palms and soles, can be induced with a variety of chemotherapeutic agents, such as capecitabine, doxorubicin, 5fluorouracil, taxanes and so on [10-12]. Compared with HFS, the incidence of dorsal hand-foot syndrome is much lower.

Albumin-bound paclitaxel (nab-paclitaxel), a novel, solvent-free taxane drug, which has demonstrated advantages in delivering a higher dose of paclitaxel to foci and reducing the incidence of severe adverse reactions. The common toxicities of nab-paclitaxel include anaphylactic reactions, myelosuppression, mucositis, fatigue and neuropathy [13].

Compared to paclitaxel and docetaxel, albumin-paclitaxel caused very few dermal toxicity reactions. Here, we report a case of dorsal HFS induced by nab-paclitaxel rather than tegeo-guided HFS. After withdrawing albumin paclitaxel, the patient's discomfort gradually eliminated and the rash did not recur. The follow-up result of this patient also authenticated that the skin toxicity was caused by albumin paclitaxel. This further reminds us that timely and accurately identify dorsal HFS is crucial for the choice of subsequent treatment. However, there is no systematic description about dorsal hand-foot syndrome from clinical symptoms, possible pathogenesis and effective managements.

First of all, in terms of diagnosis, dorsal hand and foot syndrome should be distinguished from other cutaneous toxic reactions induced with chemotherapeutic drugs, such as HFS, PATEO, HFSR and so on. In clinical symptoms characterizes: hand-foot syndrome is initially manifested as palmoplantar numbness, tingling, burning pain, and then erythema, with or without edema, desquamation. HFS is mainly founded on palms and soles that may be related to the large concentration of microcapillaries and sweat glands in these areas. PATEO showed purplish red plaques at the protrusions of large and small fish and on dorsum of hands, accompanied with nail changes that frequently progress to onycholysis. However, dorsal HFS mainly characters as symmetrical, pleomorphic purple patches, pigmentation, desquamation, with or without pain, itching and swelling appeared in the affected parts. It focuses on the dorsum of hands and rare on the dorsum of feet or around the ankle that may be related to sun-exposed [7, 14-17]. In addition to distinguishing from other dermatology toxicity caused by chemotherapeutic drugs, dorsal HFS should also be distinguished from subcutaneous bleeding caused by blood system diseases, such as thrombocytopenic purpura, leukemia and so on. They can be identified by perfecting laboratory related tests. As for histopathological characteristics, relevant studies have shown that HFS and dorsal HFS are similar. HFS's histopathological feature is hyperkeratosis of the overlying epidermis, spongiotic changes, focal vacuolization with necrotic and dyskeratotic keratinocytes in the basal cell layer. The histopathological characteristics of dorsal HFS is Keratinocyte apoptosis, dyskeratosis, atypical mitotic figures, abnormal maturation of keratinocytes [1,18,19]. In terms of occurrence mechanism, different chemotherapy drugs cause HFS by different mechanisms. The exact mechanisms governing HFS and dorsal HFS are unclear. Possible pathogenesis of HFS are as follows: C0X-2-mediated inflammatory response; chemotherapeutic drugs accumulated in small sweat ducts; enzymes related to catabolism of chemotherapeutic drugs, such as thymidine phosphorylase and Dihydropyridine Dehydrogenase (DPD) that are related to disassemble 5-FU; microcapillary damage leading to drugs extravasation and consequent dermal toxicity [14,15,20]. However, the mechanisms of dorsal HFS have not been systematically studied.

According to the types of skin toxic reactions caused by taxol, the possible pathogenesis are inflammatory reactions, solvent response and the direct cytotoxic effect. The optimal therapeutic for HFS and dorsal HFS has not yet been determined. Currently, all dermatology toxicities' managements mainly involve three aspects: patient's self-monitoring, drug treatment and chemotherapeutic dose management [21,22]. During the entire treatment, patients are advised to wear suit clothes, avoid strenuous exercise, refrain from injury and fraction of hands and feet. Except essential ways, patients with dorsal HFS are recommended to wear ice gloves, caps and avoid sun exposure [22]. In terms of symptomatic treatment measures, patients may relieve discomfort by locally using urea cream, taking medicines such as COX-2 inhibitors, pyridoxine, topical corticosteroids, vitamin E and herbal remedies [23-26]. Chemotherapeutic dose management means that when symptoms remain severe after symptomatic treatment, dose reduction or chemotherapy discontinuation may be considered [7,9]. Although the managements of other cutaneous adverse effects and dorsal HFS are similar, enhanced awareness of how to identify and treat dorsal HFS is crucial for prompt treatment and subsequent options.

Conclusion

In conclusion, this is the first case presentation of dorsal hand-foot syndrome developed by nab-paclitaxel. Currently, the mechanism and specific therapeutic measures for dorsal hand-foot syndrome have not been precisely defined, more further studies are needed to solve these problems.

How to promptly identify dorsal hand foot syndrome is pretty essential to improve the quality of life and provide duly treat strategies for patients receiving chemotherapy.

Declarations

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